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## SARS-CoV-2 vaccines and donor recruitment for FMT

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increases exponentially with age and the prevalence of comorbidity at the time of rectal cancer diagnosis is also shown to be age-related.<sup>3</sup> It is argued that 6 months of follow-up is necessary to accurately describe the mortality risk of patients aged 65 years or older who have total mesorectal excision surgery, and that this risk exceeds 10% for patients older than 75 years.<sup>3</sup> Patients aged 65 years or older who have an increased perioperative mortality risk might legitimately consider trading this upfront risk for a relatively safe, organ-preserving alternative, albeit one with a higher local failure rate of 11% at 3 years.

We appreciate that there are controversies surrounding optimal staging of patients with small rectal cancers and Mathew presents cogent arguments to support the use of endorectal ultrasound, where the aim is to discriminate T1 tumours from T2 tumours. In the TREC study, eligible patients had biopsy-proven adenocarcinoma, not greater than stage T2 on MRI, with no evidence of mesorectal lymph node metastasis. Importantly, the multidisciplinary team considered that total mesorectal excision would be the standard treatment approach. When developing the TREC study, we specifically avoided over-reliance on discrimination between T1 and T2 tumours, as accuracy across multiple sites was inconsistent.<sup>4</sup> In the TREC and STAR-TREC studies, all organ-preserving treatment schedules incorporated radiotherapy to treat potential microscopic lymph node disease. With respect to the finding of ypT3 tumours in five (19%) of 27 patients randomly assigned to organ preservation, compared with only one (4%) of 28 patients randomly assigned to total mesorectal excision, we believe that this finding reflects real-world limitations of MRI staging for discrimination of T2 from T3a rectal tumours at the time of the study, compounded by a relatively small

sample size. We were reassured that only four (7%) of 61 non-randomised organ preservation tumours were reported as ypT3. MRI reporting guidelines were provided in the protocol, supplemented by attendance of site radiologists at radiology training workshops to standardise reporting in both the TREC and STAR-TREC studies.

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- 1 Bach SP, Gilbert A, Brock K, et al. Radical surgery versus organ preservation via short-course radiotherapy followed by transanal endoscopic microsurgery for early-stage rectal cancer (TREC): a randomised, open-label feasibility study. *Lancet Gastroenterol Hepatol* 2021; **6**: 92–105.
- 2 Rombouts AJM, Al-Najami I, Abbott NL, et al. Can we save the rectum by watchful waiting or transanal microsurgery following (chemo) radiotherapy versus total mesorectal excision for early rectal cancer (STAR-TREC study)? protocol for a multicentre, randomised feasibility study. *BMJ Open* 2017; **7**: e019474.
- 3 Rutten HJT, den Dulk M, Lemmens VEPP, van de Velde CJH, Marijnen CAM. Controversies of total mesorectal excision for rectal cancer in elderly patients. *Lancet Oncol* 2008; **9**: 494–501.
- 4 Ashraf S, Hompes R, Slater A, et al. A critical appraisal of endorectal ultrasound and transanal endoscopic microsurgery and decision-making in early rectal cancer. *Colorectal Dis* 2012; **14**: 821–26.

## SARS-CoV-2 vaccines and donor recruitment for FMT

Due to its clear benefits in the management of recurrent *Clostridioides difficile* infection, faecal microbiota transplantation (FMT) has been advocated by the gastroenterological community as a non-postponable

procedure to be continuously delivered during the COVID-19 pandemic.<sup>1</sup>

Therefore, specific recommendations have been released to reorganise the workflow of FMT during the pandemic to avoid the potential risk of transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) through the FMT procedure or the donor-recipient faecal transfer.<sup>2</sup> Briefly, these recommendations included the use of remote assessment of patients and donors whenever possible, the expansion of donor screening with questionnaires and laboratory testing aimed at excluding SARS-CoV-2 infection, and the application of specific safety measures during the endoscopic FMT procedure.<sup>1,3</sup>

The SARS-CoV-2 vaccination campaign has started worldwide in the past few weeks. One major category of vaccines (developed both by BioNTech and Pfizer, and also by Moderna and the National Institute of Allergy and Infectious Diseases) is based on mRNA products that encode a genetically modified SARS-CoV-2 spike protein. These vaccines are promising, with 93–95% efficacy and minimal side-effects. An additional emerging class of vaccines, that uses a non-replicating adenovirus vector with SARS-CoV-2 spike protein, including the ChAdOx1 nCoV-19 University of Oxford and AstraZeneca vaccine, has also been given at least temporary authorisation in some countries (eg, Argentina, Brazil, and the UK, among others). Finally, various vaccine technologies, including live attenuated vaccines, are being investigated.

Overall, these efforts are expected to give a considerable boost to the fight against COVID-19. Consequently, an important discussion in the field of human tissue transfer is required, and specifically in FMT. We must consider what effect vaccination will have on FMT in clinical practice based on current knowledge and data.

The first question is whether there should be a waiting period between



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SARS-CoV-2 vaccination and donor screening. In our latest consensus report on stool biobanking, a recent history (<2 months) of vaccination with a live attenuated virus was among the exclusion criteria for stool donors in case of a possible risk of transmission.<sup>4</sup> For vaccines based on mRNA technologies (rather than live attenuated virus), it does not seem feasible that there would be a risk for transmission, and this exclusion criterion can be disregarded, as already suggested for blood donors.<sup>5</sup> Nonetheless, available vaccines have been associated with some adverse events, including fatigue, nausea, fever, headache, myalgia, arthralgia, and pain at the injection site, among others, which can last several days after the vaccination. As these symptoms can overlap with those assessed during donor screening (at the entry questionnaire and the day of each donation), it might be pragmatic to wait 7–10 days from vaccination before evaluating potential donors to avoid the risk of inappropriate rejection of candidates. It could also be reasonable to follow such an approach for vaccines based on viral vectors, as suggested in UK blood donation guidelines.<sup>6</sup> Live attenuated virus vaccines are being developed and could become available for clinical use, but we still do not have data for risk of viral transmission with these candidate vaccines. Therefore, the safest approach might be to adhere to current guidelines for this type of vaccine and wait at least 2 months after vaccination before donor screening.<sup>4</sup> At the initial evaluation, all potential donor candidates should be asked about SARS-CoV-2 vaccination and, if vaccinated, a window of time (the length depending on the type of vaccine) should elapse before moving forward with full screening (appendix).

Another question is whether donors who have been vaccinated require clinical and laboratory investigations for COVID-19 during screening. Although it is recognised that current vaccines are effective in preventing

COVID-19, uncertainty remains regarding their effect on transmission of the virus. More specifically, there are no available data for the presence of SARS-CoV-2 in the faeces of individuals who have been vaccinated if exposed, and of the risk of faecal-oral transmission of the virus. Finally, as we do not yet know how long vaccine immunity lasts, it would be difficult to predict the duration of the donor's protection against the virus. These open questions prevent any recommendation to change or streamline the current indications for the screening of stool donors, as current data do not yet assure us with a satisfactory level of safety for FMT.

Irrespective of the above considerations, because different steps of the FMT process (eg, the evaluation of donors and patients, the manipulation of faeces, the FMT procedure itself, and the follow-up of patients) could expose donors, patients, and physicians to SARS-CoV-2 infection, it is reasonable and wise to strongly encourage vaccination.

In conclusion, although the roll-out of vaccines is expected to be a turning point in the pandemic, the alert level applied to the FMT workflow to prevent the transmission of SARS-CoV-2 cannot be reduced until further data emerges.

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- 1 Ianiro G, Mullish BH, Kelly CR, et al. Screening of faecal microbiota transplant donors during the COVID-19 outbreak: suggestions for urgent updates from an international expert panel. *Lancet Gastroenterol Hepatol* 2020; **5**: 430–32.
- 2 Xiao F, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for gastrointestinal infection of SARS-CoV-2. *Gastroenterology* 2020; **158**: 1831–33.
- 3 Ianiro G, Mullish BH, Kelly CR, et al. Reorganisation of faecal microbiota transplant services during the COVID-19 pandemic. *Gut* 2020; **69**: 1555–63.
- 4 Cammarota G, Ianiro G, Kelly CR, et al. International consensus conference on stool banking for faecal microbiota transplantation in clinical practice. *Gut* 2019; **68**: 2111–21.
- 5 EUR-Lex. Commission Directive 2004/33/EC of 22 March 2004 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards certain technical requirements for blood and blood components. 2015. <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32004L0033> (accessed Jan 14, 2021).
- 6 NHS Blood and Transplant. Coronavirus: latest advice. 2020. <https://www.blood.co.uk/news-and-campaigns/news-and-statements/coronavirus-covid-19-updates/> (accessed Jan 14, 2021).



See Online for appendix

## Gastric cancer: a neglected threat to racial and ethnic minorities in the USA

The COVID-19 pandemic in the USA has exposed the pervasive inequities in health care for racial and ethnic minority groups. Health-care professionals, especially those focused on cancer prevention and early detection, were aware of this

inequity before the pandemic. But, COVID-19 has amplified the racial and ethnic health-care inequities that exist in an infrastructure that was not built to bridge these gaps, and now finds itself under pressure from an unprecedented global health crisis. Calls to rectify disparities in early cancer detection and prevention efforts are reassuring, particularly since it is anticipated that these will deepen without immediate action.<sup>1</sup> However, these calls have primarily focused on cancers for which systematic screening recommendations already exist, such as colorectal cancer and breast cancer. There is one cancer in particular that regrettably continues to get little attention, despite being defined by striking racial and ethnic disparities in the USA: gastric cancer.

Gastric cancer disproportionately affects non-White racial and ethnic minority groups in the USA, especially non-Hispanic Black Americans, Hispanic Americans, Asian Americans, and other immigrant groups coming from countries with a high incidence of gastric cancer. A recent US population-based analysis quantified this disproportionate risk, reporting that, among the age group generally considered for cancer screening (age ≥50 years), there is an up to 14.5-times higher risk of non-cardia gastric adenocarcinoma—the most common form of gastric cancer—in non-White racial or ethnic groups compared with non-Hispanic White people.<sup>2</sup> In fact, the age-adjusted incidence of gastric cancer is markedly higher than oesophageal cancer in all non-White racial or ethnic groups (appendix), and even exceeds that of colorectal cancer in certain groups (eg, Korean American men). Importantly, these comparisons probably underestimate the true burden of disease since early gastric cancer typically goes undiagnosed in the USA in the absence of systematic screening programmes.

In the USA, guidelines clearly delineate which populations are recommended to undergo screening

for colorectal and oesophageal cancers. And, because there are guidelines, these preventive interventions are typically covered by insurance. Gastric cancer screening does not have such guidelines and insurance coverage, despite substantial evidence identifying high-risk groups and decision model analyses showing that endoscopy for gastric cancer screening in these high-risk groups could be cost-effective.<sup>3</sup> Reflecting the mismatch between high disease burden in specific populations and inadequate cancer-attenuating efforts, the norm in the USA is that gastric cancer is diagnosed in more advanced stages when symptoms prompt diagnostic investigations. When diagnosed in these late stages, there are no curative options and the prognosis is dismal; this should not be the norm. In countries where gastric cancer screening programmes exist, gastric cancer is more often diagnosed in an early (typically asymptomatic) stage before submucosal invasion, when endoscopic or surgical resection can be done with curative intent and is associated with greater than 95% 5-year survival.<sup>4</sup> According to modelling studies, the cost benefit of gastric cancer screening in the USA is predominantly driven by the increased probability of diagnosing gastric neoplasia at a stage when resection is typically curative.<sup>3</sup> Moreover, there have been remarkable strides in advanced endoscopic expertise. Indeed, endoscopic resection of early gastric cancer is increasingly available in the USA,<sup>5</sup> and achieves similar outcomes as in the east Asian countries that pioneered and perfected these techniques. In fact, these techniques were borne in response to, and in parallel with, the increased number of early gastric cancer cases being diagnosed as a result of implementing national gastric cancer screening programmes in Japan and South Korea.

Thus, a convincing argument can be made that gastric cancer early